UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,550	02/09/2001	Akihiro Funakoshi	053466/0299	5276

22428 7590 01/25/2008

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
01/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/762,550	FUNAKOSHI ET AL.	
	Examiner	Art Unit	
	Lorraine Spector, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16-23,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14, 16-23, 25, 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/15/2007 has been entered.

In the response filed 8/15/2007, applicants allege that the Examiner's refusal to enter the after-final amendment filed 2/16/2007 was improper, as the dependent claims had always recited "therapeutic" method, such that the recitation of such could not raise new issues. While it is true that the dependent claims were not newly amended to contain that language, they also were not previously dependent on claim 14, but rather had previously depended from claim 15, now cancelled. While claim 15 had antecedent basis for a therapeutic method, claim 14, to which the dependency has been changed, did not. Accordingly, the Examiner's refusal to enter the amendment after final was proper.

Claims 14, 16-23, 25 and 26 are pending and under consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14, 16-23, 25 and 26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Sato et al., Cancer Research 53(4):851-6, February 1993, and/or Kishimoto et al., EP 0 791 359 A1, either or both references in view of Gross et al., Hepato-Gastroenterol. 40:522-530, cited by applicants, and Farkas et al., Neuroscience Letters 242(3):147-150. 2/20/98 for reasons of record in the previous Office Action mailed 10/6/2003.

Applicants arguments in the amendment filed 8/15/07 have been fully considered but are not deemed persuasive. At page 4 of the response, applicants argue that "That IL-6 was used as a biomarker for pancreatitis would not have motivated those of ordinary skill in the art to treat acute pancreatitis with IL-6 antagonists", on the basis that a correlation is not tantamount to a causative effect. This argument has been fully considered but is not deemed persuasive because IL-6 was not merely a biomarker, but rather would have been expected by the person of ordinary skill in the art to have a causative effect in acute pancreatitis because of its well-known property of being an *inflammatory* cytokine (for Example, see Farkas' abstract). Table 1 of Farkas clearly shows that serum IL-6 levels were greatly elevated at 4, 24 and 48 hours, compared to at 0 hours, becoming more elevated as the acute pancreatitis progressed. Gross specifically teaches that IL-6 is not only associated with, but predictive of the severity of acute pancreatitis. It simply begs credulity that these teachings would not suggest to the person of ordinary skill in the art that reduction of IL-6 levels in patients with acute pancreatitis would be beneficial. Clearly the secondary references teach that IL-6 is associated with acute pancreatitis. This, taken with the teachings of the primary reference, to use anti-IL-6 antibodies to treat IL-6 associated conditions, clearly renders obvious the claimed invention. The examiner notes that this same argument was also found non-persuasive in the Office Actions mailed 2/3/2005 and 5/24/2004.

In the response of 8/15/2007, applicants have newly submitted (but not as an information disclosure statement) a reference by Knulst, Mediators of Inflammation 3:33-40, 1994. Applicants allege that the reference "shows that in the GVHD mouse model, serum levels of IL-6 are increased, but that blocking the IL-6 using an IL-6 antibody was ineffective. This argument

has been fully considered but is not deemed persuasive because Knulst et al. conclude in the abstract that "The results of this study suggest successive waves of cytokine-secreting cell populations consistent with the induction of an inflammatory response in the development of acute GVH disease", in other words that the IL-6 was secreted only over a specific period. In contrast, the references cited by the examiner relate not to GVHD, but to acute pancreatitis, which is the subject of the claims, and teach that there is an elevated and sustained IL-6 response in acute pancreatitis. The mice used in the GVHD study had been lethally irradiated, and then "reconstituted" with spleen cells only. The full range of immune cells was not present. Knulst et al. teach at page 35 that IL-6 levels increased at day 4, and were "significantly increased" from day 5 onward. On the contrary, anti-IL-6 antibodies were injected at day 1; see page 38; while the authors state that "detectable" levels of rat IgG occurred "for a period up to 14 days", it is not clear how much of the antibody was present when IL-6 production occurred and peaked. Further, in view of Farkas' table 1, it is entirely possible that the IL-6 levels merely exceeded the amount of antibody available to such an extent that the antibody was ineffective. Knulst's conclusion of "successive waves" of cytokine production are entirely consistent with Farkas' table 1. In summary, in view of the teachings of Gross and Farkas, which deal with the actual disease in question, the teachings of Knulst et al. are not sufficient to overcome the *prima facie* finding of obviousness.

The Examiner notes that applicants continue to argue lack of a reasonable expectation of success in the face of direct teachings of administering anti-IL-6 antibodies for the purpose of counteracting the effects of excess IL-6 (Sato and Kishimoto). It is once again noted that applicants arguments are contrary to the teachings of both references. Applicants position is further belied by WO 96/40966, provided by applicants, which clearly demonstrates an expectation in the art of success at treating IL-6 associated conditions with anti-IL-6 therapeutics.

Conclusion

No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art

of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. at telephone number 571-272-0893.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Dr. Manjunath Rao, at telephone number 571-272-0939.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to **571-273-8300**. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lorraine Spector, Ph.D./
Primary Examiner, Art Unit 1647

Lorraine Spector, Ph.D.
Primary Examiner